S/N 10/696,676

NITED STATES PATENT AND TRADEMARK OFFICE

Applicant: Keith L. BLACK et al.

Examiner: Richard A. Schnizer

Serial No.: 10/696,676

Group Art Unit: 1635

Filed:

October 29, 2003

Docket:

67789-503

Title:

METHOD FOR USING POTASSIUM CHANNEL AGONISTS FOR

DELIVERING A MEDICANT TO AN ABNORMAL BRAIN REGION AND/OR

MALIGNANT TUMOR

SUPPLEMENTAL INFORMATION DISCLOSURE STATEMENT

Commissioner for Patents P.O. Box 1450 Alexandria, VA 22313-1450

In compliance with the duty imposed by 37 C.F.R. § 1.56, and in accordance with 37 C.F.R. §§ 1.97 et. seq., the referenced materials are brought to the attention of the Examiner for consideration in connection with the above-identified patent application. Applicants respectfully request that this Supplemental Information Disclosure Statement be entered and the documents listed on the attached Form 1449 be considered by the Examiner and made of record. Pursuant to the provisions of MPEP 609, Applicants request that a copy of the 1449 form, initialed as being considered by the Examiner, be returned to the Applicants with the next official communication.

Also attached hereto are copies of Forms PTO-1449 listing references discolsed by Applicants in parent application No. 09/491,500, filed January 26, 2000 (now USP 7,018,979), of which the subject application is a continuation application. Examiner is requested to acknowledge that each of these references has been reviewed in connection with the present continuation application so that these references are printed on the cover page of any patent granted on the present application.

Supplemental Information Disclosure Statement

Serial No.: 10/696,676

Filing Date: October 29, 2003

Title: METHOD FOR USING POTASSIUM CHANNEL TO SEE THE TOTAL PROBLEM TO AN ABNORMAL BRAIN REGION

AND/OR MALIGNANT TUMOR

No fee is due pursuant to 37 C.F.R. §1.97(b)(4). If additional fees are believed necessary, the Commissioner is authorized to charge any deficiency or credit any overpayment to Deposit Account No. 04-0258.

The Examiner is invited to contact the Applicants' Representative at the belowlisted telephone number if there are any questions regarding this communication.

February 21, 2007

Respectfully submitted, DAVIS WRIGHT TREMAINE LLP

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Docket No. 67789-503

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<u>CERTIFICATE UNDER 37 CFR 1.8:</u> The undersigned hereby certifies that this correspondence is being deposited with the United States Postal Service with sufficient postage as first class mail, in an envelope addressed to: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450, on this 21st day of February, 2007.

Linda B. Truong

PTO/SB/08a (08-03)

Approved for use through 07/31/2006, OMB 0651-0031
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INFORMATION DISCLOSURE STATEMENT BY APPLICANT (Not for submission under 37 CFR 1.99)

Under the Paperwork Reduction Act of 1948

Application Number		10696676		
Filing Date		2003-10-29		
First Named Inventor Keith		L. Black		
Art Unit		1635		
Examiner Name Richa		rd A. SCHNIZER		
Attorney Docket Number		67789-503		

				U.S.	PATENTS	
Examiner Initial*	Cite No	Patent Number	Kind Code ¹	Issue Date	Name of Patentee or Applicant of cited Document	Pages, Columns, Lines where Relevant Passages or Relevant Figures Appear
	1	5011837		1991-04-30	Atwal et al.	
	2	5234922		1993-08-10	Welsh et al.	
	3	7018979		2006-03-28	Black et al.	
	4	6417207		2002-07-09	Garvey et al.	
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Examiner Initial*	Cite No	Publication Number	Kind Code ¹	Publication Date	Name of Patentee or Applicant of cited Document	Pages, Columns, Lines where Relevant Passages or Relevant Figures Appear
	1	20030072748		2003-04-17	Black et al.	
	2	20020143188		2003-10-03	Garvey et al.	
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		**		FOREIGN PAT	TENT DOCUMENTS	

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Examiner Initial*	Cite No	Foreign Document Number ³	Country Code ² i	Kind Code4	Publication Date	Name of Patentee or Applicant of cited Document	Pages, Columns, Lines where Relevant Passages or Relevant Figures Appear	T5
	1	WO 01/54680			2001-02-07	Cedars-Sinai Medical Center		
	2	WO 96/12030			1996-04-25	Rhone-Poulenc Rorer S.A.		
	3	WO 01/54771			2001-08-02	Cedars-Sinai Medical Center		
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Examiner Initials*	Cite No	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc), date, pages(s), volume-issue number(s), publisher, city and/or country where published.						T 5
	1	Black, Keith L. et al., Intracarotid infusion of RMP-7, a bradykinin analog, and transport of gallium-68 ethylenediamine tetraacetic acid into human gliomas, Journal of Neurosurgery, 86(4):603-609 (1997).						
	2	Brayden, Joseph E., Functional roles of KATP channels in vascular smooth muscle, Clinical and Experimental Pharmacology and Physiology, 29(4):312-6 (2001).						
	3	Brayden, J.E., Potassium channels in vascular smooth muscle, Clinical and Experimental Pharmacology and Physiology, 23(12): 1069-76 (December 1996). (ABSTRACT ONLY)						
	4		Esaki, Takanori et al., Blockade of KATP channels with glibenclamide does not alter functional activation of cerebral blood flow in the unanesthetized rat, Brain Research, 948:56-63 (2002).					
3.	5	Hashizume, Kazuhiro et al., Increased endothelial vesicular transport correlates with increased blood-tumor barrier permeability induced by bradykinin and leukotriene C4, Journal of Neuropathology and Experimental Neurology, 61 (8):725-735 (August 2002).						

			Application Number		10696676				
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		TION DISCLOSURE	First Named Inventor	Keith	L. Black				
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	6	Inamura, Takanori et al., Bradykir Cerebral Blood Flow Metabolism,		umor b	arrier in experimental brain tumors, Journal of				
	7	Janigro, Damir et al., ATP-sensitiv Neurological Surgery, University of			in microvascular endothelial cells, Department of				
*	8	Joo, Ferenc et al., Regulation of t Research, 278:165-174 (1983).	he macromolecular transpo	rt in the	brain microvessels: the role of cyclic GMP, Brain				
	9	Liebner, Stefan et al., Claudin-1 and claudin-5 expression and tight junction morphology are altered in blood vessels of human glioblastoma multiforme, Acta Neuropathol, 100:323-331 (2000).							
	10	Liu, Sju Ming et al., Nitric oxide and cGMP regulate endothelial permeability and F-actin distribution in hydrogen peroxide-treated endothelial cells, Experimental Cell Research, 235:238-244 (1997).							
	11	Shah, Shrenik P. et al., Drug deliv Pharmaceutical Science, 6(2):252		ystem:	a review, Journal of Pharmacy and				
	12	Morimoto, Takashi et al., Increase 8:2933-2938 (September 2002).	ed levels of tissue endostation	n in hun	nan malignant gliomas, Clinical Cancer Research,				
	13	Nilaver, Gajanan et al., Delivery of herpesvirus and adenovirus to nude rat intracerebral tumors after osmotic bloodbrain barrier disruption, Proceedings of the National Academy of Science, 92:9829-9833 (October 1995).							
	14	Ningaraj, Nagendra S. et al., Adenosine 5'-triphosphate-sensitive potassium channel-mediated blood-brain tumor barrier permeability increase in a rat brain tumor model, Cancer Research, 63:8899-8911 (December 15, 2003).							
	15	Ningaraj, Nagendra S. et al., Calc brain tumor barrier, Drug News Po			s as a target protein for modulation of the blood-).				
	16				Ca2+-activated K+ channels in high Ca2+ I Physiology, 114:93-124 (July 1999).				

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	17	Schoch, Heike J. et al., Hypoxia-induced vascular endothelial growth factor expression causes vascular leakage in the brain, Brain, 125:2549-2557 (2002).	
	18	Stewart, Patrica A., Endothelial vesicles in the blood-brain barrier: are they related to permeability?, Cellular and Molecular Neurobiology, 20(2):149-163 (2002).	
12.1	19	Sugita, Masao et al., Cyclic GMP-specific phosphodiesterase inhibition and intracarotid bradykinin infusion enhances permeability into brain tumors, Cancer Research, 58(5):914-920 (1998).	
\$. X	20	Tanaka, Yoshio et al., Molecular constituents of maxi Kca channels in human coronary smooth muscle: predominant a + B subunit complexes, Journal of Physiology, 502(3):545-557 (1997).	
	21	Yokoshiki, Hisashi et al., ATP-sensitive K+ channels in pancreatic, cardiac, and vascular smooth muscle cells, Invited Review, Department of Molecular and Cellular Physiology, College of Medicine, University of Cincinnati, Cincinnati, Ohio, C25-C37 (1998).	
	22	Mackic, Jasmina B. et al., Cereport (RMP-7) increases the permeability of human brain microvascular endothelial cell monolayers, Pharmaceutical Research, 16(9):1360-1365 (1999).	
	23	Asotra, Kamlesh et al., Blood-brain barrier as portal for drug delivery, Advances in Clinical Neuroscience, 10:323-339 (2000).	
	24	Uchida, Mikito et al., Cyclic GMP-dependent blood-brain tumor barrier permeability is not mediated by cyclic GMP-dependent protein kinase, Congress of Neurological Surgeons, San Antonio, TX (2000). (ABSTRACT ONLY)	
	25	Ransom, Christopher et al., BK channels in human glioma cells, Journal of Neurophysiology, 85:790-803 (2001).	
	26	Abdul, M. and Hoosein, N., Expression and activity of potassium ion channels in human prostate cancer, Cancer Letters, 186(1):99-105 (December 1, 2002). (ABSTRACT ONLY)	
	27	Abdul, M. and Hoosein, N.M., Voltage-gated potassium ion channels in colon cancer, Oncology Report, 9(5):961-964 (September-October 2002). (ABSTRACT ONLY)	

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28	Abdul, M. et al., Activity of potassium channel-blockers in breast cancer, Anticancer Research, 23(4):3347-3351 (July-August 2003). (ABSTRACT ONLY)	
29	Baba, T. et al., Intracarotid infusion of lekotriene C4 selectively increases blood-brain barrier permeability after focal ischemia in rats, Journal of Cerebral Blood Flow and Metabolism, 11:638-643 (July 1991). (ABSTRACT ONLY)	
30	Black, Keith L., Biochemical opening of the blood-brain barrier, Advance Drug Delivery Reviews, 15:37-52 (1995).	
31	Black, Keith L., Imaging and drug delivery to tumor-infiltrated brain, Clinical Neurosurgery, Chapter 30: 563-572	
32	Black, Keith L. et al., Increased opening of blood-tumor barrier by leukotriene C4 is dependent on size of molecules, Neurological Research, 14: 402-404, (1992).	
33	Black, Keith L., Leukotriene C4 receptors in isolated brain capillaries, Advances in Prostaglandin Thromboxane and Leukotriene Research, 17:508-511(1987).	
34	Black, Keith L., Leukotrienes increase blood-brain barrier permeability following intraparenchymal injections in rats, Annals of Neurology, 18:3 349-351 (1985).	
35	Black, Keith L., Selective opening of blood-brain barrier for drug delivery to brain tumors, Perspectives in Neurological Surgery, 4:1 97-104 (1993).	
36	Chio, C.C. et al., Selective blood-tumor barrier disruption by leukotrienes, Journal of Neurosurgery, 77(3):407-410 (September 1992). (ABSTRACT ONLY)	
37	Cloughesy, T.F. et al., Intra-arterial carboplatin chemotherapy for brain tumors: a dose escalation study based on cerebral blood flow, Journal of Neuro-Oncology, 35(2):121-131 (November 1997). (ABSTRACT ONLY)	
38	Cloughesy, T.F. et al., Intra-arterial cereport (RMP-7) and carboplatin: a dose escalation study of recurrent malignant gliomas, Neurosurgery, 44(2):270-279 (February 1999). (ABSTRACT ONLY)	
	30 31 32 33 34 35 36	August 2003). (ABSTRACT ONLY) Baba, T. et al., Intracarotid infusion of lekotriene C4 selectively increases blood-brain barrier permeability after focal ischemia in rats, Journal of Cerebral Blood Flow and Metabolism, 11:638-643 (July 1991). (ABSTRACT ONLY) Black, Keith L., Biochemical opening of the blood-brain barrier, Advance Drug Delivery Reviews, 15:37-52 (1995). Black, Keith L., Imaging and drug delivery to tumor-infiltrated brain, Clinical Neurosurgery, Chapter 30: 563-572 Black, Keith L. et al., Increased opening of blood-tumor barrier by leukotriene C4 is dependent on size of molecules, Neurological Research, 14: 402-404, (1992). Black, Keith L., Leukotriene C4 receptors in isolated brain capillaries, Advances in Prostaglandin Thromboxane and Leukotriene Research, 17:508-511(1987). Black, Keith L., Leukotrienes increase blood-brain barrier permeability following intraparenchymal injections in rats, Annals of Neurology, 18:3 349-351 (1985). Black, Keith L., Selective opening of blood-brain barrier for drug delivery to brain tumors, Perspectives in Neurological Surgery, 4:1 97-104 (1993). Chio, C.C. et al., Selective blood-tumor barrier disruption by leukotrienes, Journal of Neurosurgery, 77(3):407-410 (September 1992). (ABSTRACT ONLY) Cloughesy, T.F. et al., Intra-arterial carboplatin chemotherapy for brain tumors: a dose escalation study based on cerebral blood flow, Journal of Neuro-Oncology, 35(2):121-131 (November 1997). (ABSTRACT ONLY)

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	39	Elliot, P.J. et al., Unlocking the blood-brain barrier: a role for RMP-7 in brain tumor therapy, Experimental Neurology, 141(2):214-224 (October 1996). (ABSTRACT ONLY)	
	40	Lui, Y. et al., Correlation between bradykinin-induced blood-tumor barrier permeability and B2 receptor expression in experimental brain tumors, Neurological Research, 23(4):379-387 (June 2001). (ABSTRACT ONLY)	
	41	King, Wesley A. et al., Intracarotid infusion of leukotriene C4 increases blood-tumor barrier permeability in experimental rat brain tumors, Neurological Surgery Surgical Forum, Volume XL:490-493 (1989).	
	42	Matsukado, K. et al., Steroids decrease uptake of carboplatin in rat gliomas - uptake improved by intracarotid infusion of bradykinin analog, RMP-7, Acta Neurochirurgica Supplement, 70:159-161 (1997). (ABSTRACT ONLY)	
	43	Matsukado, K. et al., Intracarotid low dose bradykinin infusion selectively increases tumor permeability through activation of bradykinin B2 receptors in malignant gliomas, Brain Research, 792(1):10-15 (May 4, 1998). (ABSTRACT ONLY)	
	44	Nakano, S. et al., Enhanced cytokines delivery and intercellular adhesion molecule 1 (ICAM-1) expression in glioma by intracarotid infusion of bradykinin analog, RMP-7, Neurological Research, 19(5):501-508 (October 1997). (ABSTRACT ONLY)	
	45	Nomura, T. et al., Intracarotid infusion of bradykinin selectively increases blood-tumor permeability in 9L and C6 brain tumors, Brain Research, 659(1-2):62-66 (October 3, 1994). (ABSTRACT ONLY)	
	46	Riley, M.G. et al., Intraarterial administration of carboplatin and the blood brain barrier permeabilizing agent, RMP-7: a toxicological evaluation in swine, Journal of Neuro-Oncology, 36(2):167-178 (January 1998). (ABSTRACT ONLY)	
	47	Sugita, M. et al., Nitric oxide and cyclic GMP attenuate sensitivity of the blood-tumor barrier permeability to bradykinin, Neurological Research, 20(6):559-563 (September 1998). (ABSTRACT ONLY)	
	48	Woodford, K.A. et al., Inhibition of ATP-sensitive potassium channels causes reversible cell-cycle arrest in human breast cancer cells in tissue culture, Journal of Cell Physiology, 162(2):163-171 (February 1995). (ABSTRACT ONLY)	
If you wis	h to a	dd additional non-patent literature document citation information please click the Add button	

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Examiner Initials*	Cite No	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc), date, pages(s), volume-issue number(s), publisher, city and/or country where published.	T5
:	4A	Bang et al., Nitroglycerin-medicated vasorelaxation is modulated by endothelial calcium-activated potassium channels, Cardiovascular Research, 43(3):772-778 (August 15, 1999). (ABSTRACT ONLY)	
	50	Black, Keith L. et al., Selective opening of the blood-tumor barrier by intracarotid infusion of leukotriene C4, Journal of Neurosurgery, 72(99):912-916 (1990).	
	51	Butt, E. et al., Inhibition of cyclic GMP-dependent protein kinase-mediated effects by (Rp)-8-bromo-PET-cyclic GMPS, British Journal of Pharmacology, 116(8): 3110-3116 (December 1995). (ABSTRACT ONLY)	
	52	Chen, C.H. et al., Nitric oxide activates Ca2+-activated K+ channels in cultured bovine adrenal chromaffin cells, Neuroscience Letters, 248(2):127-129 (May 29, 1998). (ABSTRACT ONLY)	
i de la companya de l	53	Ferrero, R. et al., Comparative effects of several nitric oxide donors on intracellular cyclic GMP levels in bovine chromaffin cells: correlation with nitric oxide production, British Journal of Pharmacology, 127(3):779-787 (June 1999). (ABSTRACT ONLY)	
	54	Fullerton, D.A. et al., Effective control of pulmonary vascular resistance with inhaled nitric oxide after cardiac operation, Journal of Thoracic Cardiovascular Surgery, 111(4):753-762; discussion 762-763 (April 1996). (ABSTRACT ONLY)	
	55	Gbadegesin, M. et al., Hypoxia modulated nitric oxide-induced regulation of NMDA receptor currents and neuronal cell death, American Journal of Physiology, 277(4 Pt 1):C673-683 (October 1999). (ABSTRACT ONLY)	
	' 5 <i>lø</i>	Goto, K. et al., Sympathetic control of arterial membrane potential by ATP-sensitive K(+)-channels, Hypertension, 35 (1 Pt 2):379-384 (January 2000) (ABSTRACT ONLY)	
	51	Hardy, P. et al., A major role for prostacyclin in nitric oxide-induced ocular vasorelaxation in the piglet, Circulation Research, 83(7): 721-729 (October 5, 1998) (ABSTRACT ONLY)	
	58	Jackson, W.F. et al., Prostacyclin-induced vasodilation in rabbit heart is mediated by ATP-sensitive potassium channels, American Journal of Physiology, 264(1 Pt 2):H238-43 (January 1993) (ABSTRACT ONLY)	

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	Kieler-Jensen, N. et al., Inhaled nitric oxide in the evaluation of heart transplant candidates with elevated pulmonary vascular resistance, Journal of Heart and Lung Transplant, 13(3): 366-375 (May-June 1994) (ABSTRACT ONLY)						
	60		A. et al., Mode of nitric oxide action on the renal vasculature, Acta Physiologica Scand, 168(1): 41-45 (January (ABSTRACT ONLY)				
	او		et al., Hypoxic dilation of porcine small coronary arteries: role of endothelium and KATP-channels, British of Pharmacology, 120(4):728-734 (February 1997) (ABSTRACT ONLY)				
	Patel, A.I. et al., Activation of guanosine 3', 5'-cyclic monophosphate (cGMP)-dependent protein kinase in rat vas deferens and distal colon is not accompanied by inhibition of contraction, Journal of Pharmacology and Experimental Therapeutics, 283(2): 894-900 (November 1994) (ABSTRACT ONLY)						
	<i>υ</i> 3	Patel, A.I. and Diamond, J., Activation of guanosine 3', 5'cyclic monophosphate (cGMP)-dependent protein kinase in rabbit aorta by nitroglycerin and sodium nitroprusside, Journal of Pharmacology and Experimental Therapeutics, 283 (2):885-893 (November 1997) (ABSTRACT ONLY)					
	Rajek, A. et al., Inhaled nitric oxide reduces pulmonary vascular resistance more than prostaglandin E(1) during heart transplantation, Anesthesia and Analgesia, 90(3): 523-530 (March 2000) (ABSTRACT ONLY)						
	Solina, A. et al., A comparison of inhaled nitric oxide and milrinone for the treatment of pulmonary hypertension in adult cardiac surgery patients, Journal of Cardiothoracic Vascular Anesthesia, 14(1):12-17 (February 2000) (ABSTRACT ONLY)						
	Vaali, K. et al., Relaxing effects of NO donors on guinea pig trachea in vitro are mediated by calcium-sensitive potassium channels, Journal of Pharmacology and Experimental Therapeutics, 286(1): 110-114 (July 1998) (ABSTRACT ONLY)						
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Application Number 10696676 Filing Date 2003-10-29 INFORMATION DISCLOSURE Keith L. Black First Named Inventor STATEMENT BY APPLICANT Art Unit 1635 (Not for submission under 37PCER 1.99) **Examiner Name** Richard A. SCHNIZER Attorney Docket Number 67789-503 **CERTIFICATION STATEMENT** Please see 37 CFR 1.97 and 1.98 to make the appropriate selection(s): That each item of information contained in the information disclosure statement was first cited in any communication from a foreign patent office in a counterpart foreign application not more than three months prior to the filing of the information disclosure statement. See 37 CFR 1.97(e)(1). OR That no item of information contained in the information disclosure statement was cited in a communication from a foreign patent office in a counterpart foreign application, and, to the knowledge of the person signing the certification after making reasonable inquiry, no item of information contained in the information disclosure statement was known to any individual designated in 37 CFR 1.56(c) more than three months prior to the filing of the information disclosure statement. See 37 CFR 1.97(e)(2). fact to See attached certification statement. Fee set forth in 37 CFR 1.17 (p) has been submitted herewith. **SIGNATURE** A signature of the applicant or representative is required in accordance with CFR 1.33, 10.18. Please see CFR 1.4(d) for the form of the signature. 2007-02-21 Signature Date (YYYY-MM-DD) Name/Print Linda B. Truong Registration Number 56461 This collection of information is required by 37 CFR 1.97 and 1.98. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR

This collection of information is required by 37 CFR 1.97 and 1.98. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 1 hour to complete, including gathering, preparing and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. **SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.**

April 18, 2000

Sheet 1 of 5

FOR 1449°		
INFORMATION	DISCLOSURE	STATEMENT

OPE 40

IN AN APPLICATION

(Use several sheets if necessary)

Docket Number: CEDAR 043453

Application Number:

R 043453 09/491,500

Applicant: Keith L. Black and Nagendra S. Ningaraj

Filing Date: Jan. 26, 2000 Group Art Unit: 1646

U.S. PATENT DOCUMENTS							
EXAMINER INITIAL	DOCUMENT NO.	DATE	NAME	CLASS	SUBCLASS	FILING I	OATE OPRIATE
	5,112,596	05/12/92	Malfroy-Camine				
	5,124,146	06/23/92	Neuwelt				
	5,215,985	06/01/93	Murphy et al.				····
	5,234,947	08/10/93	Cherksey				·· · · · · · · · · · · · · · · · · ·
	5,256,688	10/26/93	Grover et al.				•
	5,262,419	11/16/93	Aberg et al.				
	5,268,164	12/07/93	Kozarich et al.				
	5,314,887	05/24/94	Aldrich et al.				
	5,399,587	03/21/95	Garcia et al.				
	5,416,097	05/16/95	Erhardt et al.				
	5,434,137	07/18/95	Black				
	5,527,527	06/18/96*	Friden				
	5,527,778	06/18/96°	Black				-
	5,578,599	11/26/96	Diani et al.				
	5,604,198	02/18/97	Podusio et al.				
	5,670,477	09/23/97	Poduslo et al.				
	5,677,344	10/14/97	Greenfield et al.				
	5,679,706	10/21/97	D'Alonzo et al.				
	5,686,416	11/11/97*	Kozarich et al.				
· .	5,695,751	12/09/97	Friedman et al.			·····	
	5,760,230	06/02/98	Schohe-Loop et al.				
	5,869,509	02/09/99	Romine et al.			· · · · · · · · · · · · · · · · · · ·	
	5,922,735	07/13/99	Sit et al.				•
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	DOCUMENT NO.	DATE	COUNTRY	CLASS	SUBCLASS	TRANS	LATION
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DATE CONSIDERED

FORM 1449° INFORMATION DISCLOSURE STATEMENT	Docket Number: CEDAR 043453	Application Number: 09/491,500	
IN AN APPLICATION	Applicant: Keith L. Black and Nagendra S. Ningaraj		
(Use several sheets if necessary)	Filing Date: Jan. 26, 2000	Group Art Unit: 1646	

	OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, Etc.)
1.	Adeagbo, A.S., 1-Ethyl-2-benzimidazolinone stimulates endothelial K(Ca) channels and nitric oxide formation in rat mesenteric vessels, Eur. J./ Pharmacol, 379(2-3):151-9 (August 27, 1999). ABSTRACT ONLY.
2.	Akar, F., et al., <i>Protective effect of cromakalim and diazoxide, and proulcerogenic effect of glibenclamide on indomethacin-induced gastric injury</i> , <u>Eur. J. Pharmacol</u> , 374(3):461-70 (June 25, 1999). ABSTRACT ONLY.
3.	Andrade, S.P., et al., <i>Pharmacological reactivity of neoplastic and non-neoplastic associated neovasculature to vasoconstrictors</i> , <u>Int. J. Exp. Pathol</u> , 79(6):425-32 (December 1998). ABSTRACT ONLY.
4.	Brian, J.E., Jr., et al., Recent insights into the regulation of cerebral circulation, Clin. Exp. Pharmacol Physiol, 23(6-7):449-57 (June-July 1996). ABSTRACT ONLY.
5.	Brismar, T., et al., <i>Mechanism of high K+ and TI+ uptake in cultured human glioma cells</i> , <u>Cell Mol. Neurobiol</u> , 15(3):351-60 (June 1995). ABSTRACT ONLY.
6.	Brismar, T., et al., <i>Thallium-201 uptake relates to membrane potential and potassium permeability in human glioma cells</i> , <u>Brain Res.</u> , 500(1-2):30-6 (October 23, 1989). ABSTRACT ONLY.
 7.	Burg, M.A., et al., NG2 proteoglycan-binding peptides target tumor neovasculature, Cancer Res., 59(12):2869-74 (June 15, 1999). ABSTRACT ONLY.
 8.	Burrows, F. J., et al., Eradication of large solid tumors in mice with an immunotoxin directed against tumor vasculature, Proc. Natl. Acad. Science U.S.A., 90(19):8996-9000 (October 1, 1993). ABSTRACT ONLY.
9.	Butt, A.M., Effect of inflammatory agents on electrical resistance across the blood-brain barrier in pial microvessels of anaesthetized rats, Brain Res., 696(1-2):145-50 (October 23, 1995). ABSTRACT ONLY.
10.	Butt, A.M., et al., Effect of histamine and antagonists on electrical resistance across the blood-brain barrier in rat brain-surface microvessels, Brain Res., 569(1):100-5 (January 8, 1992). ABSTRACT ONLY.
11.	Cai, S., et al., Single-channel characterization of the pharmacological properties of the K(Ca2+) channel of intermediate conductance in bovine aortic endothelial cells, J. Membr. Biol., 163(2):147-58 (May 15, 1998). ABSTRACT ONLY.
12.	Chang, S.S., et al., Five different anti-prostate-specific membrane antigen (PSMA) antibodies confirm PSMA expression in tumor-associated neovasculature, Cancer Res., 59(13):3192-8 (July 1, 1999). ABSTRACT ONLY.
13.	Chaplin, D.J., et al., Anti-vascular approaches to solid tumour therapy: evaluation of combretastatin A4 phosphate, Anticancer Res., 19(1A):189-95 (JanFeb. 1999). ABSTRACT ONLY.

EXAMINER	DATE CONSIDERED	٦
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FÖRM 1449° INFORMATION DISCLOSURE STATEMENT	Docket Number: CEDAR 043453	Application Number: 09/491,500	
IN AN APPLICATION	Applicant: Keith L. Black and Nagendra S. Ningaraj		
(Use several sheets if necessary)	Filing Date: Jan. 26, 2000	Group Art Unit: 1646	

14.	Chassande, O., et al., The Na+/K+/Cl- cotransport in C6 glioma cells, Properties and role in volume regulation, Eur. J. Biochem., 171(3):425-33 (February 1, 1988). ABSTRACT ONLY.
15.	Chess-Williams, R., et al., In vitro investigation of the bladder-vascular selectivity of levcromakalim and YM934 in human tissues, <u>BJU Int.</u> , 83(9):1050-4 (June 1999). ABSTRACT ONLY.
16.	Dark, G.G., et al., Combretastatin A-4, an agent that displays potent and selective toxicity toward tumor vasculature, Cancer Res., 57(10):1829-34 (May 15, 1997). ABSTRACT ONLY.
17.	Denekamp, J., et al., Vasculature and microenvironmental gradients: the missing links in novel approaches to cancer therapy? Adv. Enzyme Regul., 38:281-99 (1998). ABSTRACT ONLY.
18.	Desai, S.B., et al., <i>Tumor angiogenesis and endothelial cell modulatory factors</i> , <u>J. Immunother</u> , 22(3):186-211 (May 1999). ABSTRACT ONLY.
19.	D'hahan, N., et al., A transmembrane domain of the sulfonylurea receptor mediates activation of ATP-sensitive K(+) channels by K(+) channel openers, Mol. Pharmacol, 56(2):308-15 (August 1999). ABSTRACT ONLY.
20.	Duda, T., Mutations in the Rod Outer Segment Membrane Guanylate Cyclase in a Cone-Rod Dystrophy Cause Defects in Calcium Signaling, Biochemistry, 38(42):13912-13919 (October 19, 1999). ABSTRACT ONLY.
21.	Faraci, F.M., et al., Responses of cerebral arterioles to N-methyl-D-aspartate and activation of ATP-sensitive potassium channels in old rats, Brain Res., 654(2):349-51 (August 22, 1994). ABSTRACT ONLY.
22.	Faraci, F.M., et al., <i>Potassium channels and the cerebral circulation</i> , Clin. Exp. Pharmacol Physiol, 23(12):1091-5 (December 1996). ABSTRACT ONLY.
23.	Friebe, A., et al., <i>Mechanism of YC-1-induced activation of soluble guanylyl cyclase</i> , <u>Mol. Pharmacol</u> , 53(1):123-7 (January 1998). ABSTRACT ONLY.
24.	Goldstein, G. W., et al., In vitro studies of the blood-brain barrier using isolated brain capillaries and cultured endothelial cells, Ann. N.Y. Acad. Science, 481:202-13 (1986). ABSTRACT ONLY.
25.	Harland, S. P., et al., Expression of enthothelin(A) receptors in human gliomas and meningiomas, with high affinity for the selective antagonist PD156707, Neurosurgery, 43(4):890-8; discussion 898-9 (October 1998). ABSTRACT ONLY.
. 26.	Holland, M., et al., Effects of the BKCa channel activator, NS1619, on rat cerebral artery smooth muscle, Br. J. Pharmacol, 117(1):119-29 (January 1996). ABSTRACT ONLY.
27.	Jain, R. K., Vascular and interstitial barriers to delivery of therapeutic agents in tumors, Cancer Metastasis Rev., 9(3):253-66 (November 1990). ABSTRACT ONLY.
28.	Keep, R. F., et al., <i>Potassium transport at the blood-brain and blood-CSF barriers</i> , <u>Adv. Exp.</u> Med. Biol., 331:43-54 (1993). ABSTRACT ONLY.

	EXAMINER	DATE CONSIDERED
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FORM 1449° INFORMATION DISCLOSURE STATEMENT	Docket Number: Application Number: CEDAR 043453 09/491,500		
in an application	Applicant: Kelth L. Black and Nagendra S. Ningaraj		
(Use several sheets if necessary)	Filing Date: Jan. 26, 2000	Group Art Unit: 1646	

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29.	Konoshita, H., et al., Differential effects of lidocaine and mexiletine on relaxations to ATP-sensitive K+ channel openers in rat aortas, Anesthesiology, 90(4):1165-70 (April 1999). ABSTRACT ONLY.
30.	Kitazono, T., et al., Role of potassium channels in cerebral blood vessels, Stroke, 26(9):1713-23 (September 1995). ABSTRACT ONLY.
31.	Lee, Y.S., et al., In vitro antitumor activity of cromakalim in human brain tumor cells, Pharmacology, 49(2):69-74 (August 1994). ABSTRACT ONLY.
32.	Manor, D., et al., Interactions among calcium compartments in C6 rat glioma cells; involvement of potassium channels, J. Physiol. (Lond.), 478(Pt.2):251-63 (July 15, 1994). ABSTRACT ONLY.
33.	Miller, T.R., et al., <i>Pharmacological and molecular characterization of ATP-sensitive K+channels in the TE671 human medulloblastoma cell line</i> , <u>Eur. J. Pharmacol</u> , 370(2):179-85 (April 9, 1999). ABSTRACT ONLY.
34.	Molema, G., et al., <i>Tumor vascular endothelium: barrier or target in tumor directed drug delivery and immunotherapy</i> , <u>Pharm. Res.</u> , 14(1):2-10 (January 1997). ABSTRACT ONLY.
35.	O'Donnell, M.E. et al., Cerebral microvascular endothelial cell Na-K-Cl cotransport: regulation by astrocyte-conditioned medium, Am. J. Physiol., 268(3 Pt. 1):C747-54 (March 1995). ABSTRACT ONLY.
36.	Ohizumi, I., et al., Antibody-based therapy targeting tumor vascular endothelial cells suppresses solid tumor growth in rats, Biochem Biophys. Res. Commun., 236(2):493-6 (July 18, 1997). ABSTRACT ONLY.
. 37.	Ohta, Y., et al., <i>Tumor angiogenesis and recurrence in stage I non-small cell lung cancer</i> , Ann. Thorac. Surg., 68(3):1034-8 (September 1999). ABSTRACT ONLY.
38.	Panchal, R.G., Novel therapeutic strategies to selectively kill cancer cells, Biochem Pharmacol., 55(3):247-52 (February 1, 1998). ABSTRACT ONLY.
39.	Patel, H.J., et al., Inhibition of cholinergic neurotransmission in guinea pig trachea by NS1619, a putative activator of large-conductance, calcium-activated potassium channels, J. Pharmacol. Exp. Ther., 286(2):952-8 (August 1998). ABSTRACT ONLY.
40.	Ran, S., et al., Infarction of solid Hodgkin's tumors in mice by antibody-directed targeting of tissue factor to tumor vasculature, Cancer Res., 58(20):4646-53 (October 15, 1998). ABSTRACT ONLY.
41.	Redrobe, J.P., et al., The effect of the potassium channel activator, cromakalim, on antidepressant drugs in the forced swimming test in mice, Fundam. Clin. Pharmacol., 10(6):524-8 (1996). ABSTRACT ONLY.
42.	Rettig, W.J., et al., Identificatgion of endosialin, a cell surface glycoprotein of vascular endothelial cells in human cancer, Proc. Natl. Acad. Sci. U.S.A., 89(22):10832-6 (November 15, 1992). ABSTRACT ONLY.

EXAMINER	
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DATE CONSIDERED

FORM 1449° INFORMATION DISCLOSURE STATEMENT	Docket Number: CEDAR 043453	Application Number: 09/491,500	
IN AN APPLICATION	Applicant: Keith L. Black and Nagendra S. Ningaraj		
(Use several sheets if necessary)	Filing Date: Jan. 26, 2000	Group Art Unit: 1646	

43.	Revest, P.A., et al., The transendothelial DC potential of rat blood-brain barrier vessels in situ, Adv. Exp. Med. Biol., 331:71-4 (1993). ABSTRACT ONLY.
44.	Revest, P.A., et al., <i>Transendothelial electrical potential across pial vessels in anaesthetised rats: a study of ion permeability and transport at the blood-brain barrier</i> , Brain Res., 652(1):76-82 (July 25, 1994). ABSTRACT ONLY.
45.	Sandstrom, P.E., et al., Identification of potassium flux pathways and their role in the cytotoxicity of estramustine in human malignant glioma, prostatic carcinoma and pulmonary carcinoma cell lines, Eur. J. Cancer, 30A(12):1822-6 (1994). ABSTRACT ONLY.
46.	Schilling, L., et al., Opening of the blood-brain barrier during cortical superfusion with histamine, Brain Res., 653(1-2):289-96 (August 8, 1994). ABSTRACT ONLY.
47.	Serfass, L., et al., Effect of heme oxygenase inhibitors on soluble guanylyl cyclase activity, Arch. Biochem. Biophys., 359(1):8-16 (1998). ABSTRACT ONLY.
48.	Sobey, C.G., et al., Mechanisms of bradykinin-induced cerebral vasodilatation in rats. Evidence that reactive oxygen species activate K+ channels, Stroke, 28(11):2290-4; discussion 2295 (November 1997). ABSTRACT ONLY.
49.	Smoak, I.W., Cromakalim: embryonic effects and reduction of tolbutamide-induced dysmorphogenesis in vitro, Teratology, 60(5):260-264 (November 1999). ABSTRACT ONLY.
50.	Sugai, K. et al., Levcromakalim decreases cytoplasmic Ca2+ and vascular tone in basilar artery of SAH model dogs, J. Cardiovasc. Pharmacol., 33(6):868-75 (June 1999). ABSTRACT ONLY.
51.	Teramoto, N. et al., Comparative studies on the relaxing action of several adenosine 5'-triphosphate-sensitive K+ channel openers in pig urethra, J. Smooth Muscle Res., 35(1):11-22 (February 1999). ABSTRACT ONLY.
52.	Thorpe, P. E. et al., Antibody-directed targeting of the vasculatlure of solid tumors, Breast Cancer Res. Treat., 36(2):237-51 (1995). ABSTRACT ONLY.
53.	Toyoda, K. et al., Role of ATP-sensitive potassium channels in brain stem circulation during hypotension, Am. J. Physiol., 273(Pt. 2):H1342-6 (September 1997). ABSTRACT ONLY.
54.	Van Hinsbergh, V. W. et al., Angiogenesis and anti-angiogenesis: perspectives for the treatment of solid tumors, Ann. Oncol., 10 Supl 4:60-3 (1999). ABSTRACT ONLY.
55.	Walter, J. J. et al., Angiostatin binds to smooth muscle cells in the coronary artery and inhibits smooth muscle cell proliferation and migration In vitro, Arterioscler. Throm. Vasc. Biol., 19(9):2041-8 (September 1999). ABSTRACT ONLY.
56.	Wickenden, A.D. et al., Comparison of the effects of the K(+)-channel openers cromakalim and minoxidil sulphate on vascular smooth muscle, Br. J. Pharmacol., 103(1):1148-52 (May 1991). ABSTRACT ONLY.

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	EXAMINER	DATE CONSIDERED	
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FORM PTO-1449 (Modified)	ATTY DOCKET NO.	SERIAL NO.	
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U.S. PATENT DOCUMENTS

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	WO 00/23102	27.04.00	PCT				
	0 351 767 A2	24.01.90 Bul. 90/04	EP				
	0 555 681 A1	18.08.93 Bul. 93/33	EP				
	0 575 749 A2	29.12.93 Bul. 93/52	EP				-

OTHER ART (Including Author, title, Date, Pertinent Pages, Etc.)

57.	XP-002195899 - Oak, Z. et al., Effects of Cyclic GMP on Microvascular Permeability of the Cerebral Cortex, Microvascular Research, Vol. 58, pp. 35-40
58.	(1999). XP-002195900 - Role of nitric oxide in histamine-induced increases in permeability of the blood-brain barrier,
 59.	Mayhan, William G., Brain Research, Vol. 743, pp. 70-76 (1996). XP-002195901 - Bartus, R. T. et al., Controlled Modulation of BBB Permeability Using the Bradykinin Agonist,
60.	RMP-07, Experimental Neurology, Vol. 142, pp. 14-28 (1996). International Search Report re PCT/US01/02743,P mailed 26/04/2002

EXAMINER	DATE CONSIDERED;
EXAMINER: Initial if citation considered, whether or not citation	
not in conformance and not considered. Include copy of this form	with next communication to applicant.

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	AA	5,518,499	05/21/06	Agar				
	AB	5,767,160	06/16/98					
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	AC	Brain Res, 799	9:44-48 (199	98). ABS7	a channel activation to hyp FRACT ONLY.			
	AD	Barna, M., et a infection, Viro			III nitric oxide synthase in 6 996).	astrocytes fo	llowing a neu	rotropic viral
	AE				r-stimulated phosphoprotein I Cardiovasc Pharmacol, 35			
	AF	Boje, K.M., In meningitis, <u>Br</u>			e synthase attenuates blood 83 (1996).	l-brain barr	ier disruption	during experimental
	AG	Brandt, L., et a microvasculat Metabolism, 3	ure under n	ormal con	pplication of calcium antag ditions and in focal ischem	gonist (nifed ia, <u>Journal o</u>	ipine) on felin f Cerebral Bl	ne cortical pial ood Flow and
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	AI	Bychkov, R., e coronary arter	et al. <i>Calicu</i> ries, <u>J Phara</u>	m-activate acol Exp T	d potassium channels and i herap, 285:293-8 (1998).	nitrate-indu ABSTRACT	ced vasodilati ONLY.	ion in human
	AJ	Chandran, S.,	et al., <i>Nitric</i>	oxide: con	ncepts, current perspectives	and future	therapeutic ii	mplications, <u>Indian</u>
	Journal of Pharmacology, 30:351-366 (1998). AK Chi, O.Z., et al. Effect of inhibition of nitric oxide synthase on blood-brain barrier transport in focal cerebral ischemia, Pharmacologylogy, 48:367-373 (1994).							
	AL Cloughesy, T.F., et al., Pharmacological blood-brain barrier modification for selective drug delivery, Journal of Neuro-Oncology, 26:125-132 (1995).							
	AM		The use of n	itric oxide	donors in pharmacologica	l studies, <u>Na</u>	unyn-Schmie	deberg's Arch
	AN				ndent protein kindase active Plation at serine 1072, <u>J Bi</u> c			
	AO	Fukumura, D., Metastasis Rey			xide in angiogenesis and m	icrocirculat	ion in tumors	, Cancer and

EXAMINER

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AQ

DATE CONSIDERED

He, P., et al., cGMP modulates basal and activated microvessel permeability independenty of [Ca2+]i, Am J

Herrera, G.M., et al., Maintained vasodilatory response to cromakalim after inhibition of nitric oxide

EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

synthesis, J Cardiovasc Pharmacol, 31:921-9 (1998). ABSTRACT ONLY

Physiol, 274:H1865-74 (1998). ABSTRACT ONLY.

FORM	PTO-	1449,	Adapted

LIST OF INFORMATION DISCLOSED BY APPLICANT (Use several sheets if necessary)

ATTY. DOCKET NO.	SERIAL NO. 09/491,500	FILING DATE January 26, 2000	
APPLICANT Keith L. Black and Nagendra S. Ningaraj		GROUP 1632	
	OTHER REFERENCES (Inc.	luding Author, Title, Date, Pertinent Pages, Etc.)	
AR		of cGMP in modulation of macromolecule permeability of aortic 2:H91-8 (1997). ABSTRACT ONLY.	
AS	Hongli, X., et al., Opening blood-brain-barrier by intracarotid infusion of papaverine in treatment of malignant cerebral glioma, Chinese Medical Journal, 111(8):751-753 (1998).		
AT	Hurst, R.D., et al., Nitric oxide-induced perturbations in a cell culture model of the blood-brain barrier, Journal of Cellular Physiology, 167:89-94 (1996).		
AU	Inamura, T., et al., Intracarotid histamine infusion increases blood tumour permeability in RG2 glioma, Neurological Research, 16:125-128 (1994).		
AV	Inamura, T., et al., Intracarotid infusion of RMP-7, a bradykinin analog: a method for selective drug delivery to brain tumors, J. Neurosurg, 81:752-758 (1994).		
AW	Janigro, D., et al., Regulation of blood-brain barrier endothelial cells by nitric oxide, Circulation Research, 75:528-528 (1994).		
AX	Kimura, M., et al., Responses of human basilar and other isolated arteries to novel nitric oxide donors, <u>J</u> Cardiovasc Pharmacol, 32: 695-701 (1998). ABSTRACT ONLY.		
AY	Koesling, D., Modulators of soluble guanylyl cyclase, Naunyn-Schmiedeberg's Arch Pharmacol, 358:123-126 (1998).		
AZ	Liu, Y., et al., Repeated, short-term ischemia augments bradykinin-mediated opening of the blood-tumor barrier in rats with RG2 glioma, Neurological Research, 23:631-639 (2001).		
BA	Lohse, M.J., et al., <i>Pharmacology of NO:cGMP signal transduction</i> , Naunyn-Schmiedeberg's Arch Pharmcol 358:111-112 (1998).		
ВВ	Matukado, T., et al., Selective Increase in Blood Tumor Permeability by Calcium Antagonists in Transplanted Brain Tumors, Acta Neurochir, 60: 403-405 (1994).		
BC	Mayer, B., et al., Nitric oxide synthases: catalytic function and progress toward selective inhibition, Naunyn-Schmiedeberg's Arch Pharmcol, 358:127-133 (1998).		
BD	Mayhan, W.G., Role of nitric oxide in histamine-induced increases in permeability of the blood-brain barrier, Brain Research, 743:70-76 (1996).		
BE	Mayhan, W.G., et al., Glutamate-induced disruption of the blood-brain barrier in rats, Stroke, 27:965-970 (1996).		
BF	Nakano, S., et al., Increased brain microvessel permeability after intracarotid bradykinin infusion is mediated by nitric oxide, Cancer Research, 56:4027-4031 (1996).		
BG	Ningaraj, N.S., et al., Role of ATP-sensitive K+ channels in blood-brain tumor barrier permeability, Congress of Neurological Surgeons Annual Meeting, 50 th Anniversary Celebration, September 23-28, 2000, Henry B. Gonzalez Convention Center, San Antonio, Texas, ABSTRACT No. 4309, p. 215.		
EXAMINER .		DATE CONSIDERED	

conformance and not considered. Include copy of this form with next communication to applicant.

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LIST OF INFORMATION DISCLOSED BY APPLICANT

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	OTHER	REFERENCES (Inclu	ding Author, Title, Date, Pertinent Pages, Etc.)
ВН	BH Ningaraj, N.S., et al., Ca2+-dependent K+ channels are a key regulatory of blood-brain tumor barrier permeability, Congress of Neurological Surgeons Annual Meeting, 50 th Anniversary Celebration, September 23-28, 2000, Henry B. Gonzalez Convention Center, San Antonio, Texas, ABSTRACT No.428, p. 219.		
BI	Ningaraj, N.S., et al., Nitric oxide donors increase blood-brain tumor barrier permeability via Kca channels, Society for Neuroscience, 30 th Annual Meeting, New Orleans, LA, November 4-9, 2000, 26 Part 1, p. 338, ABSTRACT No. 126.8.		
BJ	Ningaraj, N.S., et al., Regulation of blood-brain tumor barrier permeability by calcium-activated potassium channels, The Journal of Pharmacology, June 2002, 301: 838-851		
BK	Pardrige, W., et al., Blood-brain barrier and new approaches to drug delivery, West J Med, 156:281-286 (1992).		
BL	Robertson, B.E., et al., cGMP-dependent protein kinase activates Ca-activated K channels in cerebral artery smooth muscle cells, Am J Physiol, 265:C299-C303 (1993).		
BM	Sobey, C.G., et al., Inhibitory effect of 4-aminopyridine on responses of the basilar artery to nitric oxide, Br J Pharmacol, 126:1437-43 (1999). ABSTRACT ONLY.		
BN	Salom, J.B., et al., Relaxant effects of sodium nitroprusside and NONOates in rabbit basilar artery, Pharmacology, 57:79-97 (1998). ABSTRACT ONLY.		
ВО	Salom, J.B., et al., Comparative relaxant effects of the NO donors sodium nitroprusside, DEA/NO and SPER/NO in rabbit carotid arteries, Gen Pharmacol, 32:75-59 (1999). ABSTRACT ONLY.		
BP	Salom, J.B., et al., Relexant effects of sodium nitroprusside and NONates in goat middle cerebral artery: delayed impairment of global ischemia-reperfusion, Nitric Oxide, 3:85-93 (1999). ABSTRACT ONLY.		
BQ	Shukla, A., et al., Nitric oxide-dependent blood-brain barrier permeability alteration in the rat brain, Experientia, 52:136-140 (1996).		
BR	Smolenski, A., et al., Functional analysis of cGMP-dependent protein kinases I and II as mediators of NO/cGMP effects, Naunyn-Schmiedeberg's Arch Pharmacol, 358:134-138.		
BS	Sugita, M., et al., Cyclic GMP-specific phosphodiesterase inhibition and intracarotid bradykinin infusion enhances permeability in brain tumors, Cancer Research, 58:914-920 (1998).		
BT	Takayasu, M., et al., Effects of calcium antagonists on intracerebral penetrating arteriolesi in rats, <u>J. Neurosurg</u> , 69:104-109 (1988).		
BU	Uchida, M., et al., Overexpression of bradykinin type 2 receptors on glioma cells enhances bradykinin-mediated blood-brain tumor varrier permeability increase, Neurological Research, 24:739-745		
EXAMINER			DATE CONSIDERED
			ion is in conformance with MPEP 609; Draw line through citation if not in ext communication to applicant.

	Adapted

LIST OF INFORMATION DISCLOSED BY APPLICANT

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APPLICANT Keith L. Black and Nagendra S. Ningaraj		GROUP 1632	
	OTHER REFERENCES (Inc.	luding Author, Title, Date, Pertinent Pages, Etc.)	
BV	Uchida, M., et al., Cyclic GMP-dependent blood-brain tumor barrier permeability is not mediated by cyclic GMP-dependent protein kinase, Congress of Neurological Surgeons Annual Meeting, 50 th Anniversary Celebration, September 23-28, 2000, Henry B. Gonzalez Convention center, San Antonio, Texas, ABSTRACT No. 440, p. 220.		
BW	Vodovotz, Y., et al., Regulation of transforming growth factor beta 1 by nitric oxide, Cancer Res, 59:2142-9 (1999). ABSTRACT ONLY.		
BX	Yukabu, M.A., Hematoma-induced enhanced cerebral vasoconstriction to leukotriene C4 and endothelin-l piglets: role of prostanoids, Pediatr Res, 38:119-23 (1995). ABSTRACT ONLY.		
BY	Tocris Web Page, http://www.tocris.com/cat/nodonorstxt.html No Donors/Precursors, pp.1-2, Downloaded 5/31/00.		
BZ	Sigma-Aldrich Web page, http://vsearch.sial.com/search 97cgi/s97-cgi, p.1, downloaded 5/31/00.		
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